PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	29.05.2001
Applicant's or agent's file reference RCD/P32080WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/00517	17/02/2000	18/02/1999

Applicant
UNIVERSITY OF LEEDS et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hanrieder-Kreuzer, K Tel.+49 89 2399-8081

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
RCD/P32080WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/00517	17/02/2000	18/02/1999
International Patent Classification (IPC) or national classification and IPC A61K7/06		
Applicant UNIVERSITY OF LEEDS et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18/09/2000	29.05.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Renoth, H Telephone No. +49 89 2399 8589

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00517

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-18	as originally filed				
Claims, No.:					
1-25	as received on	01/03/2001	with letter of	27/02/2001	
Drawings, sheets:					
1/6-6/6	as originally filed				

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 19,20,25.

because:

   ☒ the said international application, or the said claims Nos. 19,20,25 with respect to industrial application relate to the following subject matter which does not require an international preliminary examination (*specify*): **see separate sheet**

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

   Novelty (N) Yes: Claims 1-10,22-24

	No:	Claims	11-18,21
Inventive step (IS)	Yes:	Claims	1-10,22-24
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18,21-24
	No:	Claims	19,20,25

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

ITEM III

Claims 19, 20 and 25 disclose subject-matter to the use of a compound in medical treatment and methods of therapeutical treatment of a human or animal body. Claims 19, 20 and 25, thus, relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the subject-matter of these claims (Article 34(4)(a)(i) PCT).

ITEM V

The following documents cited in the international search report are considered to be relevant with respect to the subject-matter of the present application;

D1: US-A-5 679 329 (DUPUIS ET AL.) 21 October 1997 (1997-10-21)

D2: CH 686 998 A (PARFUMS GIVENCHY) 30 August 1996 (1996-08-30)

D3: EP-A-0 850 642 (L'OREAL) 1 July 1998 (1998-07-01)

D4: ZAGALSKY ET AL.: 'The quaternary structure of the lobster carapace...' COMP. BIOCHEM. PHYSIOL., B: COMP. BIOCHEM., vol. 97B, no. 4, 1990, pages 837-848, XP000913411

D5: LEE ET AL.: 'Crosslinking of tissue-derived biomaterials...' JOURNAL MATERIALS SCIENCE, vol. 7, no. 9, 1996, pages 531-541, XP000907368

D6: VERHEUL ET AL.: 'Association behavior of native beta-lactoglobulin' BIOPOLYMERS, vol. 49, no. 1, 1999, pages 11-20, XP002140160

D7: SHAHAN ET AL.: 'Expression of six mouse major urinary protein genes ...' MOL. CELL. BIOL., vol. 7, no. 5, 1987, pages 1947-54, XP000913409

Novelty, Article 33(2) PCT

1. Independent claim 1 of the present application discloses the use of calycin for targeting a ligand to hair fibre and/or skin surface.

   Although it is known from D1 that calycins like milk proteins contain a domain for binding to hair fibres, it is not disclosed in any of the documents cited in the international search report that calycins can be used as a carrier for ligands functioning as a coupling agent bound to the ligand and the hair fibre and/or skin surface to target the ligand to the hair fibre and/or skin surface.

2. The subject-matter of independent claim 22 (1. medical use) is not mentioned in any of the documents cited in the international search report.

3. Claims 2-10 and 23, 24 are dependent on independent claims 1 and 22 respectively, and as such also meet the requirements of the PCT with respect to novelty and inventive step.

4. Though not explicitly disclosed in any of the documents of the international search report, a method for creating calycin or a calycin multimer comprising the use of recombinant DNA techniques, as defined in independent claim 11 and dependent claims 12-18 of the present application, is well known in the art (cf. present application, page 7, 3rd full paragraph). Therefore, there is no need for such a document.

5. The use of a hair care composition which involves the targeting of the calycin to hair to provide a conditioning effect is disclosed in D1.

Inventive step (Article 33(3) PCT)

6. D1 is considered to be the most relevant prior art. The object of D1 is to overcome the phenomenon of powdering and the instability of foams which are generated through the use of milk proteins in hair care products.

7. The present application is concerned with the targeting of a ligand to hair or skin surface by exploiting the ligand binding domain of a calycin. D1 does not disclose the ligand binding domain of a calycin.
The skilled person faced with the problem of the present application would obtain no guidance from D1 that would lead him to the solution of the present invention.

8. In the documents of the international search report there is no hint that calycin could be bound to a therapeutic agent for use as a medicament.

9. Independent claims 1 and 22 as well as dependent claims 2-10, 23 and 24 are, thus, considered to involve an inventive step.

Industrial application, Article 33(4) PCT

According to claims 19, 20 and 25 and the description pages 8 (4th full paragraph) and 9 (2nd to 4th paragraph) the composition of the present application is not solely directed to cosmetical use but also to a pharmaceutical use.
For the assessment of the present claims 19, 20 and 25 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

ITEM VI

The following documents is considered to become relevant in the regional examination proceedings:

Pupl. No.:	WO-A-99/16873
Applic. No.:	PCT/DE 98/02898
Priority date:	26.09.1997 (DE 19742706.5)
Filing date:	25.09.1998
Puplic. date:	08.04.1999

Furthermore, should the present application not be entitled to priority, the above mentioned document and the following article
CHATEL ET AL.: 'Expression of a Lipocain in Prokaryote and Eukaryote cells...' PROTEIN EXPRESSION PURIFICATION, vol. 16, no. 1, June 1999 (1999-06), pages 70-75, XP000913408 (cited in the international search report) will become relevant with respect to the state of the art.

ITEM VIII

Due to the very broad definition of claim 1 and considering the description the it is not unambiguously clear whether the subject-matter of claims 1-10 excludes medical treatments.

CLAIMS

1. Use of a calycin comprising a binding domain for binding at least one selected ligand and a targeting domain that binds to at least a part of a hair fibre and/or skin surface for targeting said ligand to said hair fibre and/or skin surface.

2. Use of claim 1 wherein the calycin further comprises an interaction domain which interacts with a such a domain on another calycin whereby they associate.

3. Use of claim 2 wherein the calycin is selected from a fusion protein and is a multimer.

4. Use of any of claims 1 to 3 wherein said binding domain and/or said targeting domain is endogenous to the calycin or calycin multimer.

5. Use of any of claims 1 to 3 wherein said binding domain and/or said targeting domain is adapted by alteration of the endogenous binding and/or targeting domain or by substitution of the endogenous binding and/or targeting domain for a domain that has the required functionality.

6. Use of any of claims 1 to 5 wherein said binding domain is adapted to bind more than one ligand.

7. Use of a claim 6 wherein the ligands bind to different respective binding domains found in different naturally occurring calycins.

8. Use of any of claims 1 to 7 wherein the or at least one calycin has the ablility to bind fatty acids that coat hair cuticles and/or skin or protein moieities that comprise the cuticle and/or skin.

9. Use of any of the preceding claims wherein the or at least one calycin is ß-lactoglobulin.

10. Use of any of claims 1 to 8 wherein the or at least one calycin is Major Urinary Protein and/or recombinant Major Urinary Protein.

11. A method for creating a calycin, optionally a calycin multimer, which is as defined in any of the preceding claims and is a mutant or fusion protein, wherein said method comprises the use of recombinant DNA techniques in the creation of the calycin mutant and fusion proteins.

12. A method according to claim 11 wherein the ligand binding domain and/or the targeting domain is genetically modified to alter the specificity of ligand binding and/or the affinity of the targeting domain for its binding site.

13. A method according to claim 11 and/or claim 12 wherein the calycin comprises a molecular complex with more than one type of ligand binding domain, wherein calycin genes are fused to one another and/or appropriate linking regions are used to produce a multi component gene and gene product and/or interaction sites are introduced into individual monomers of the calycins such that on mixing the individual proteins, molecules assemble into multi-sub unit complexes with similar or different functionalities.

14. A method according to claim 11 and/or claim 12 wherein said method comprises chemical methods in the crosslinking of calycin monomers to form multimeric complexes.

15. A method of claim 13 further comprising a method of claim 14.

16. A method of claim 14 or 15 wherein said chemical methods include the use of a bifunctional cross-linking agent.

17. A method of claim 16 wherein the cross-linking agent is 1-ethyl-3-[3-dimethylaminopropyl]cardodiimide hydrochloride (EDC).

18. A method of claims 11 to 17 to effect the cross-linking of ß-Lactoglobulin and recombinant Major Urinary Protein.

19. Use of a hair or skin care composition comprising at least one calycin as defined in any of claims 1 to 10.

20. Use according to claim 19 wherein said composition provides a cosmetic or therapeutic effect.

21. Use according to claim 20 wherein the cosmetic effect involves the targeting of said calycin to hair to provide a conditioning effect and/or the targeting of perfume or hair dye to hair to provide at least one desired effect.

22. A calycin bound to a therapeutic agent for use as a medicament.

23. A calycin according to claim 22 wherein the medicament is a veterinary composition for use in the treatment of parasitic infection of animals and/or birds.

24. A calycin according to claim 22 wherein the calycin binds and transports an insecticide to hair and/or skin to prevent and/or cure infestation.

25. A method for the treatment of humans and/or animals and/or birds which involves the administration of a composition comprising a calycin to an individual and/or animal and/or bird to prevent and/or cure a condition affecting hair, fur, hide, feathers, scalp and skin.